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CASE REPORT

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Management of weight loss in a patient with Prader-Willi syndrome with satietogenics: a case report

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Abstract

Objective: To report the evolution and therapeutic approach in a patient with PraderWilli Syndrome (PWS) associated with literature data assessment with a focus on the pharmacological treatment of obesity in patients with this pathology, since there are currently not many studies that contribute or name a strategy with the use of satietogenics. **Methods:** The present study was elaborated according to the rules of CARE case report. Due to the cognitive impairment present in the syndrome, the patient's mother was first contacted about the writing of this paper and was given consent through the signing of the Free and Informed Assent Term for this paper. The patient was treated at a hospital-adjacent Nutrology outpatient clinic in 2019. **Case Description:** YSP, 20 years old, diagnosed with PWS and Grade III obesity (initial BMI of 55.4kg/m², 140kg) attended the Nutrology outpatient clinic of Adriano Jorge Hospital Foundation – FHAJ in 2019 under referral from a third party, and his companion (relative) reporting hyperphagia and poor school performance, initially without a nutrition plan, during follow-up, nutritional guidance and multi-professional care have been initiated. **Results:** During the follow-up of the years 2019-2021, resulting from the SARS-CoV-2 pandemic in Brazil and the consequent confinement, the patient presented worsening anxiety and hyperphagia, evolving with increased binge eating and discontinuation of physical activities and diet adherence. During the follow-up in the same period, there were 03 returns denoting weight maintenance, later (2021) the use of on-label (Sibutramine), off-label (Fluoxetine), and Metformin medications were associated with the therapeutic regimen for obesity, due to evidence of insulin resistance. **Final considerations**: The patient evolved with progressive weight loss and better adherence to the food plan and physical activities.

Keywords: Prader-Willi syndrome. Obesity. Satiety. Satietogenics drugs.

Introduction

Prader-Willi Syndrome (PWS) is a multisystem disease of dominant inheritance, in addition to obesity in early childhood, other manifestations include infantile hypotonia, hypogonadism, cognitive deficits, and below-normal stature for age. Obesity in patients with this syndrome is associated with hyperphagia (sometimes leading to gastric rupture) and foraging for food. Such hyperphagia and cognitive disorders are major obstacles in weight management in an outpatient setting, requiring frequent follow-ups and family members' emotional support **[1,2]**.

In addition to the patient's willingness to pursue the therapeutic objective. Therefore, the study aims to report the evolution and therapeutic approach in a

patient with PWS associated with data collection in literature with a focus on the pharmacological approach to obesity in patients with this pathology, since there are currently not many studies that contribute to or name a main strategy with the use of satietogenic drugs.

Methods

Study Design

The present study was elaborated according to the rules of CARE case report. Available in: https://www.care-statement.org/.

Ethical Approval

The case report refers to a 20-year-old patient being followed up at a tertiary facility, in a hospital-adjacent Nutrology outpatient clinic. Authorization was expressly obtained through the Free and Informed Consent Term and the Consent Term for the Use of Documents signed by the patient. This study was analyzed and approved by the Research Ethics The committee from Fundação Hospital Adriano Jorge (Adriano Jorge Hospital Foundation - FHAJ), Manaus, Amazonas, Brazil, through approval opinion number 5.596.676.

Case Report

Patient Information and Clinical Findings

YSP, 20 years old, diagnosed with PWS and Grade III obesity (initial BMI of 58.6 kg/m², 140.8 kg) attended FHAJ Nutrology outpatient clinic in 2019 under referral from a third party, with a companion reporting hyperphagia and poor performance in school, initially without a nutritional diet plan. During follow-up, nutritional guidelines were initiated and multiprofessional referrals were given. During the follow-up in the years 2019-2021, resulting from the SARS-CoV-2 pandemic in Brazil and the consequent social confinement, the patient showed worsening anxiety and hyperphagia, evolving with increased binge eating and discontinuation of physical activities and adherence to a diet. During the follow-up in the same period, there were 03 returns denoting weight maintenance. Due to the cognitive impairment characteristic of the syndrome, information was obtained with permission from his main guardian and relative (mother), under the signature of TFCA (Term of Free and Clarified Assent) and TCUD (Term of Commitment to Use Data).

During the first months of follow-up, both the patient and relatives were given nutritional guidelines with a dietetic plan with a goal of negative energy balance with an allowance of roughly 1.5 g of protein/kg of ideal body weight (IBW) and 1.500 kcal, besides behavioral orientations (such as underexposure to foods of all kinds with a focus on the hypercaloric kind, reduction of sucrose intake and often reminders/incentives for physical activity). After the first appointment, the patient was referred to the services of Psychology, Endocrinology, and Neurology provided by the healthcare unit where this study took place.

During his subsequent follow-ups (**Table 1**), both on-label (Sibutramine, 15mg PO q.d) and off-label (Fluoxetine, 20mg PO q.d) medications were added to enhance weight loss and, with Metformin later added because of clinically and laboratoryconfirmed insulin resistance observed during his Endocrinology follow-up. Later Fluoxetine was replaced with Buproprione 150mg PO q.d by the Neurologist's feedback. After said adjustments the patient maintained stable weight (with no observed increases bigger than 5% during subsequent follow-ups), and no adverse effects related to the satietogenics were noticed either.

Table 1. Anthropometric data during the follow-up period (2019-2022).

	Weight (Kg)	BMI (kg/m²)
Nov. 2019	140.8	58.6
Jan. 2020	138.1	57.4
Jul. 2020	141.2	58.7
Aug. 2020	140.6	58.5
Apr. 2021	130.6	54.6
Mai. 2021	126.2	52.5
Jun. 2021	118.3	49.2
Aug. 2021	110.0	45.7
Oct. 2021	110.0	45.7
Jan. 2022	109.3	45.4
Mar. 2022	108.3	45.1

Source: Own authorship.

Discussion

Prader-Willi Syndrome (PWS) is a genetic inheritance syndrome that causes neurobehavioral and structural alterations **[1]**, being the main genetic syndrome causing obesity, which, in turn, is an important cause of morbidity and mortality, mostly related to cardiovascular incidents **[3-7]**.

Amongst some of the clinical manifestations of PWS, the hallmark of the disease and the focus of this article is hyperphagia with the consequent obesity. It's been classically described as having two nutritional phases: poor feeding and failure to thrive in infancy (First phase), followed by hyperphagia and obesity in late childhood and teenage years (Second phase) **[6]**,

with later studies proposing a phase zero characterized by decreased fetal movements and growth restriction **[8-10]**.

Said hyperphagia hasn't been completely clarified yet, although some recent studies have proposed several mechanisms behind it **[11-16]**. One of them comparing healthy pediatric patients with those with PWS have shown increased levels of fasting ghrelin, with an interesting negative link between total ghrelin versus age and weight gain in both groups, with roughly half of the PWS patients exhibiting below average weightfor-age z-score15, hypothesized by food intake restriction from their parents, adding a theory that hyperghrelinaemia might induce weight gain in patients with an independent food intake control (i.e late childhood and onwards) **[17]**.

Another study compared neural mechanisms between PWS and healthy individuals, even though the hypothalamus plays a central role in regulating food intake, no structural abnormalities or distinct pre/post-meal activation patterns were found amongst PWS patients **[18]**. And, recently, a fMRI (functional magnetic resonance imaging) study of three PWS individuals showed a mean signal reduction latency of 24 minutes after glucose injection when compared to the 15-minute delay in obese individuals, providing evidence of dysfunction in the neural satiety mechanisms in patients with PWS **[19]**.

In the present study, the patient already was clinically diagnosed with PWS before his first appointment, and with the characteristics shown in the literature of obesity, hyperphagia, and poor school performance, possibly related to the cognitive deficit characteristic of the syndrome **[1-3]**. Considering this and the importance of the intervention due to the risks of obesity for the patient's life **[1-4]**, a nutritherapy plan was initiated and later followed by pharmacotherapy with satietogenic drugs **[20]**. The latter approach is the highlight of this paper, given that the literature is scarce regarding the use of anti-obesity drugs, although there is some information on the use of fluoxetine, topiramate, mazindol **[5]**.

Fluoxetine is a selective serotonin reuptake inhibitor (SSRI) whose approved indications are major depression, obsessive behaviors, and panic disorders; with an offlabel use for weight loss due to its effect on blocking the reuptake of serotonin (which has been linked to reduced food intake), increasing it's extracellular concentration. Fluoxetine, alongside other serotonergic drugs, also appears to block hunger signals from neuropeptide Y (an orexigenic peptide) by inhibiting its action in the hypothalamic paraventricular nucleus **[20,21]**.

Also, sibutramine, despite being a drug used to treat obesity, is not routinely used in PWS. It is a medication that acts on satiety and in addition to being a dual reuptake inhibitor of norepinephrine and serotonin (whose effects were discussed earlier), it can have positive effects in reducing impulsive behavior. Norepinephrine's role in weight loss lies in its induction of triglycerides lipolysis, reducing white adipose tissue mass while preventing a decline in metabolic rate associated with hypocaloric diets **[5]**.

In this case, sibutramine and fluoxetine were initially prescribed, in addition to Metformin, as PWS is commonly associated with insulin resistance due to obesity and hormonal changes1, although some studies have proposed a weight loss aimed to use for Metformin in non-diabetic patients due to its appetite suppressing side effects, often hypothesized to be due to mild metabolic acidosis related anorexia (via lactate production) and increased secretion of GLP-1 and the anorectic hormone peptide YY **[8,13]**. This treatment allowed the patient to progress with a weight loss of 30kg and greater adherence to dietary and physical activity plans. Showing improvement in obesity, and a probable behavioral improvement due to adherence to other therapeutic plans, essential for weight maintenance **[1,3,5]**.

This paper demonstrates sibutramine as a probable therapeutic option in obesity resulting from PWS to be researched due to its effectiveness in this case, needing to be evaluated the balance between benefits and side effects, which were not noticed, in addition to the effectiveness with prolonged use of the drug medication.

Conclusion

The patient evolved with a weight loss of approximately 30kg (weight of 110.9 kg at the last follow-up) since the beginning of the pharmacotherapeutic use, with greater engagement in physical activities and, although he still refers to food impulsiveness, he has better adherence to the nutritherapy plan and remains in outpatient follow-up. No adverse effects were recorded.

Acknowledgement

Not applicable.

Ethical Approval

This study was analyzed and approved by the Research Ethics Committee from Hospital Foundation Adriano Jorge - HFAJ, Manaus-Amazonas, Brazil, through approval opinion number 5.596.676.

Informed consent

The patient alongside their legal guardian signed the consent form.

Funding

Not applicable.

Data sharing statement

No additional data are available.

Conflict of interest

The authors declare no conflict of interest.

Similarity check

It was applied by Ithenticate@.

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